89/252-522 #7 Cont

Exhibit A

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EXHIBIT A

CLAIMS PENDING IN APPLICATION SERIAL NO. 09/232,522
AS OF DECEMBER 17, 1999

1. An antibody to the human IL-12p75 heterodimer which consists of a p35 subunit and a p40 subunit wherein said antibody.

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

(b) is produced from a mouse which is deficient in the gene encoding a mouse p35 subunit or p40 subunit of IL-12.

2. The antibody of claim 1, wherein the antibody is a monoclonal antibody.

3. The antibody of claim 1, wherein the antibody is produced from a cell line of the mouse.

4. The antibody of claim 1, wherein the antibody cross-reacts with rhesus monkey IL-12.

5. The antibody of claim 1, wherein the antibody is humanized.

6. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12446.

7. The antibody of claim 6, wherein the antibody is humanized.

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8. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12447.

9. The antibody of claim 8, wherein the body is humanized.

10. The antibody of claim 1, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12448.

11. The antibody of claim 10, wherein the antibody is humanized.

12. The antibody of claim 1, wherein the antibody produced by a hybridoma having ATCC designation number HB-12449.

13. The antibody of claim 12, wherein the antibody is humanized.

14. A monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said monoclonal antibody

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any eptiope presented by said p40 subunit; and

(b) neutralizes at least about 90% of the bioactivity of human IL-12.

15. The antibody of claim 14, wherein the antibody neutralizes at least about 90% bioactivity of human IL-12 by inhibiting IL-12 stimulated PHA-activated human

lymphoblast proliferation wherein the concentration of said antibody is 0.5 μg/ml and the concentration of said human IL-12 is 0.25 ng/ml.

16. The antibody of claim 14, wherein the antibody neutralizes at least about 90% of bioactivity of human IL-12 by inhibiting IL-12 stimulated IFN-γ production wherein the concentration of the antibody is 0.5 μg/ml and the concentration of said human IL-12 is 0.25 ng/ml.

17. The antibody of claim 14, wherein the antibody cross reacts with rhesus monkey IL-12.

18. The antibody of claim 14, wherein the antibody is humanized.

19. The antibody of claim 14, wherein the antibody is produced by a hybridoma.

20. The antibody of claim 19, wherein the antibody is humanized.

21. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12446.

22. The antibody of claim 21, wherein the antibody is humanized.

23. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12447.

24. The antibody of claim 23, wherein the antibody is humanized.

25. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation/number HB-12448.

26. The antibody of claim 25, wherein the antibody is humanized.

27. The antibody of claim 14, wherein the antibody is produced by a hybridoma having ATCC designation number HB-12449.

28. The antibody of claim 27, wherein the antibody is humanized.

29. A hybridoma that is capable of producing a monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said antibody

(a) immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit; and

(b) is produced from a cell line obtained from a mouse deficient in a gene encoding a mouse p35 subunit or p40 subunit of IL-12.

30. The hybridoma of claim 29 wherein the hybridoma is HIL-12F3-5F2 having ATCC designation number HB-12446.

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31. The hybridoma of claim 29 wherein the hybridoma is HIL-12F3-16F2 having ATCC designation number HB-12447.

32. The hybridoma of claim 29, wherein the hybridoma is HIL-12F3-20E11 having ATCC designation number HB-12448.

33. The hybridoma of claim 29, wherein the hybridoma is HIL-12F3-16G2 having ATCC designation number HB-12449.

34. A method for producing an antibody that selectively immunologically reacts with the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit, comprising the steps of:

(a) immunizing a mammal deficient in a gene encoding said p35 subunit or said p40 subunit with the human IL-12 p75 heterodimer to produce antibodies;

(b) obtaining antibodies from the immunized mammal;

(c) screening said antibodies for their ability to selectively bind an epitope presented by the p75 heterodimer to obtain said selectively binding antibody.

35. A method for producing a monoclonal antibody that selectively immunologically reacts with the human IL-12 p75 heterodimer which consists of a p35 usbunit and a p40 subunit, comprising the steps of:

(a) immunizing a mammal deficient in a gene encoding said p35 subunit or said p40 subunit with the human IL-12 p75 heterodimer to produce antibodies;

(b) harvesting antibody producing cells from the immunized mammal;

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(c) forming a monoclonal antibody producing hybridoma from said cells and obtaining said monoclonal antibody;

(d) screening said monoclonal antibody produced by said hybridoma for the ability to selectively bind to an epitope presented by the p75 heterodimer to obtain said selectively binding monoclonal antibody.

36. The method of claim 35, wherein the antibodies produced from the hybridoma are futher screened and selected for their ability to cross react with rhesus monkey IL-12.